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| 10/563,042 | 03/13/2006 | Shubha Anand | BJS-620-406 | 8188 |

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NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

| EXAMINER | |
|---|---|
| LOVE, TREVOR M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1611 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/563,042 | ANAND ET AL. | |
| | Examiner | Art Unit | |
| | TREVOR M. LOVE | 1611 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/01/2010 has been entered.

Claims 1-10 are pending.

Claims 11-51 are cancelled.

Claim 10 remains withdrawn.

Claims 1-9 are currently under consideration.

### *Arguments directed to the previously presented 131 Declaration*

Applicant again argues with regard to the Rule 131 declaration filed June 8, 2009. Applicant appears to believe that "[t]he previously–filed Rule 131 Declaration is submitted to be persuasive in antedating the primary reference and reconsideration of the same is respectfully requested" (see remarks, page 6). Applicant's argument and declaration are not found persuasive since it is clear that Applicant has not met the requirements clearly set forth in MPEP 715 for antedating a reference. *For instance*, Applicant has failed to provide a clear showing wherein the "showing of facts shall be such, in character and weight, as to establish reduction to practice prior to the effective date of the reference, or conception of the invention prior to the effective date of the

reference coupled with due diligence from prior to said date to a subsequent reduction to practice or to the filing of the application. Original exhibits of drawings or records, or photocopies thereof, must accompany and form part of the affidavit or declaration or their absence must be satisfactorily explained." The Anand reference fails to identify that Applicant had possession of the full scope of the invention, for instance, the Anand reference does not even mention the active Hesperadin. Further, Applicant has not provided any showing of diligence from said date or a reduction to practice as of said date. Therefore, Applicant's arguments and declaration are not found persuasive to antedate the Hauf reference.

**Withdrawn Rejections**

The rejection of claims 1-5 and 8-9 under 35 U.S.C. 103(a) as being unpatentable over Hauf et al (Journal of Cell Biology) (IDS reference) is withdrawn in view of Applicant's amendments to the claims.

The rejection of claim 6 under 35 U.S.C. 103(a) as being unpatentable over Hauf et al (Journal of Cell Biology) (IDS reference) as set forth above for instant claims 1-5, in further view of Slamon et al (N.E.J.M.) as evidenced by Lange et al (EMBO Journal) is withdrawn in view of Applicant's amendments to the claims.

The rejection of claim 7 under 35 U.S.C. 103(a) as being unpatentable over Hauf et al (Journal of Cell Biology) (IDS reference) as set forth above for instant claims 1-5, in further view of Obermiller et al (Breast Cancer Res) as evidenced by Lange et al (EMBO Journal) is withdrawn in view of Applicant's amendments to the claims.

**New Grounds of Rejection**

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1-5 and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sen et al (1997, Oncogene) as evidenced by Entrez Gene (AURKA Aurora Kinase A) in view of Patel et al (2000, Oncogene) and Hauf et al (2003, Journal of Cell Biology) (IDS reference).**

Sen teaches that human breast cancer exhibits an amplified and overexpressed amount of BTAK which is a serine/threonine kinase (see entire document, for instance, Title). Entrez Gene evidences that BTAK is also known as aurora kinase A (see entire document, for instance section labeled "Summary").

Sen fails to directly teach treating breast cancer with an Aurora A Kinase inhibitor, namely Hesperadin, or with a mitotic spindle assembly inhibitor, namely paclitaxel.

Patel teaches that paclitaxel is a microtubule-stabilizing agent, wherein cells exit mitosis aberrantly and fractionate into hypodiploid populations during cell cycle analysis (see entire document, for instance, page 4163, first column, first paragraph). Patel further teaches that breast cancer cells are sensitive to paclitaxel (see entire document, for instance, Title).

Hauf teaches that Hesperadin is an aurora A kinase inhibitor (see entire document, for instance page 284, column 2, last paragraph). Hauf proffers that Hesperadin treatment turned off checkpoint signaling in taxol-treated cells because all kinetochores progressively accumulated stably attached microtubles. Hauf teaches that Hesperadin might allow cells treated with paclitaxel to exit the mitotic phase by

stabilizing improper microtubule attachments (see entire document, for instance page 288, column 2, last sentence).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the antineoplastic agent paclitaxel of Patel and the aurora A kinase inhibitor Hesperadin of Hauf to treat a patient with breast cancer, such as those of Sen. One would have been motivated to do so since both the paclitaxel of Patel and the Hesperadin of Hauf are directed to exiting cells from mitosis wherein the exiting cell is in an aberrant or improper condition. Further, one would have been motivated to utilize Hesperadin (a known aurora A kinase inhibitor) to inhibit the overexpression of aurora A kinase in breast cancer as taught by Sen. Also, one owuld have been motivated to utilize the paclitaxel of Patel to treat the breast cancer of Sen since Patel teaches that breast cancer cells are sensitive to paclitaxel. There would be a reasonable expectation of success since both Sen and Patel are directly drawn to breast cancer, and Sen identifies a clear nexus between aurora A kinase and breast cancer.

*Response to Arguments*

Applicant argues in the remarks filed 02/10/2010 that given the teachings of Hauf, one would expect an antagonistic effect of utilizing paclitaxel and Hesperadin in combination. Applicant's argument is not found persuasive since, as seen above, both paclitaxel and Hesperadin are directed to exiting cells from mitosis wherein the exiting cell is in an aberrant or improper condition. While the two drugs might utilize different mechanisms of action, one of ordinary skill in the art, given the teachings of Sen, Patel,

and Wang would arrive at a combination of paclitaxel and Hesperadin with a reasonable expectation that the cells would exit mitosis in an aberrant or improper condition, which is preferred for breast cancer cells. Applicant's arguments directed to the previously presented 131 declaration are addressed above.

**Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sen et al (1997, Oncogene) as evidenced by Entrez Gene (AURKA Aurora Kinase A) in view of Patel et al (2000, Oncogene) and Hauf et al (2003, Journal of Cell Biology) (IDS reference) as applied to claims 1-5 and 8-9 above, and further in view of Slamon et al (N.E.J.M.).**

The teachings of Sen, Patel, and Hauf are set forth above.

Sen fails to directly teach the presence of an antibody which is an aurora A kinase inhibitor.

Slamon teaches that recombinant monoclonal antibody are useful in breast cancer patients to aid in correcting the over expression of HER2 which is over-expressed in 25 to 30% of breast cancers (see Abstract, first eight lines).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize antibodies to mediate the over-expression of aurora A kinase in the breast cancer patients of Sen. One would have been motivated to do so since Slamon teaches the mediation of HER2 over-expression in breast cancer patients by the utilization of antibodies. There would be a reasonable expectation of success in the combination since Applicant identified in the instant specification that there are

many well known methods of acquiring antibodies (see instant specification, page 7, lines 1-13). Furthermore, Sen teaches that aurora A kinase is over-expressed in breast cancer patients, and Slamon teaches that antibodies can be used to mediate over-expression of HER2. One would have looked to various options to overcome the aurora A kinase over-expression, such as antibodies. One would have particularly looked to antibodies since Slamon teaches a method of reducing HER2 gene over-expression by using antibodies (see Slamon (see page 783, last paragraph through 784, first paragraph).

*Response to Arguments*

Applicant argues in the remarks filed 02/10/2010 that Slamon fails to cure the deficiencies alleged above in Hauf. Applicant's arguments are not found persuasive. See above response to arguments.

**Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sen et al (1997, Oncogene) as evidenced by Entrez Gene (AURKA Aurora Kinase A) in view of Patel et al (2000, Oncogene) and Hauf et al (2003, Journal of Cell Biology) (IDS reference) as applied to claims 1-5 and 8-9 above, and further in view of Obermiller et al (Breast Cancer Res).**

The teachings of Sen, Patel, and Hauf are set forth above.

Sen fails to directly teach the presence of a sense or anti-sense nucleic acid which is an aurora A kinase inhibitor.

Obermiller teaches that gene therapy is useful when trying to correct specific molecular defects that contribute to the cause or progression of cancer, specifically, breast cancer (see abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize sense or anti-sense nucleic acids to mediate the over-expression of aurora A kinase in the breast cancer patients of Sen. One would have been motivated to do so since Obermiller teaches that gene therapy provides the ability to correct specific molecular defects that contribute to the cause or progression of cancer, this would include the over-expression of aurora A kinase in breast cancer patients. There would be a reasonable expectation of success in the combination since Applicant identified in the instant specification that there are many well known methods of down-regulating gene expression. Specifically, the instant specification states "[T]he use of these approaches [sense and anti-sense] to down-regulate gene expression is now well-established in the art (see instant specification, page 8, lines 6-9 and page 10, lines 21-27).

*Response to Arguments*

Applicant argues in the remarks filed 02/10/2010 that Obermiller and Lange fail to cure the deficiencies alleged above in Hauf. Applicant's arguments are not found persuasive. See above response to arguments.

## ***Conclusion***

No claims allowed. All claims rejected. No claims objected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TREVOR M. LOVE whose telephone number is (571)270-5259. The examiner can normally be reached on Monday-Thursday 7:30-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TL

/David J Blanchard/
Primary Examiner, Art Unit 1643